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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,248	11/27/2006	Yuji Okubo	Q96497	4347

23373 7590 05/11/2009

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EXAMINER	
SHEN, WU CHENG WINSTON	

ART UNIT	PAPER NUMBER
1632	

MAIL DATE	DELIVERY MODE
05/11/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,248	OKUBO ET AL.	
	Examiner	Art Unit	
	WU-CHENG Winston SHEN	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *1-19 and 26-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 August 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :08/31/2006, 11/27/2006, 07/12/2007, and 10/15/2007.

DETAILED ACTION

This application 10/591,248 filed on 11/27/2006 is a 371 of PCT/JP2005/003589 filed on 03/03/2005. This application claims foreign priority of JAPAN 2004-061291 filed on 03/04/2004, and JAPAN 2004-062812 filed on 03/05/2004.

Election/Restriction

Applicant's election with traverse of Group X, claims 20-25, drawn a yeast transformant which is introduced with a polyhydroxyalkanoic acid synthase gene and an acetoacetyl CoA reductase gene, and both of these genes being introduced in 2 or more copies, in the reply filed on 02/24/2009 is acknowledged. The traversal is on the ground(s) that claim 20 is not anticipated by Remacha because Remacha does not disclose the yeast transformant of claim 22. Applicant furthermore argues that since claims 26-33 depend from claim 20, they should be examined together with claim 20. In the event the Examiner finds that claims 26-33 should be examined together with claim 20, Applicant elects amino acid substitution (a) of claim 27. The traversal is not found persuasive because as previously stated in the restriction, the inventions listed as Groups I-XXVI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Applicant's claims encompass multiple inventions, multiple products (various yeast transformants) and multiple methods (methods of making and methods of using the products), and do not have a special technical feature which link the inventions one to the other, and lack unity of invention. The common technical feature in all groups is a yeast transformant. However, this common technical feature cannot be a special technical feature

under PCT Rule 13.2 because the feature is shown in the prior art. Remacha et al. teaches that by gene disruption techniques with linearized DNA from these constructions, strains of *Saccharomyces cerevisiae* were obtained which lacked a functional gene for either protein L44 or protein L45.

Applicant states that it appears to Applicant that the content of Groups XI, XIII, XV, XVII, XIX, XX, XXII, and XXIV, as indicated at pages 4 -7 of the Office Action, does not correspond to the recitation of each claim. In response, the Examiner notes that the contents of these Groups are not verbatim of the claims because yeast transformants with different genomic compositions, including exchromosomal gene(s) introduced, are considered as distinct inventions (products), which have been clearly indicated and restricted into different groups.

With regard to requirement to elect a species, Applicant elects *Candida maltosa* for examination, and claims 1-36 are readable on the elected species. It is noted that election of *Candida maltosa* as species reads on the *Candida* genus recited in claim 23, and the *maltosa* species listed in claim 24. Applicant states that if any of the elected claims is found to be allowable, claims dependent therefrom should similarly be considered allowable in the same application, and Applicant reserves the right to file a Divisional Application directed to non-elected non-rejoined claims. In response, the Examiner notes that the potential rejoinder has been documented on page 10 of the office action mailed on 12/24/2008, and is reiterated below.

MPEP 1893.03(d) Unity of Invention Rejoinder

MPEP 1893.03(d) states: If an examiner (1) determines that the claims lack unity of invention and (2) requires election of a single invention, when all of the claims drawn to the elected invention are allowable (i.e., meet the requirements of 35 U.S.C. 101, 102, 103 and 112),

the nonelected invention(s) should be considered for rejoinder. Any nonelected product claim that requires all the limitations of an allowable product claim, and any nonelected process claim that requires all the limitations of an allowable process claim, should be rejoined. See MPEP § 821.04 and § 821.04(a). Any nonelected processes of making and/or using an allowable product should be considered for rejoinder following the practice set forth in MPEP § 821.04(b).

Claims 1-36 are pending.

Claims 1-19 and 26-36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 01/29/2009.

Claims 20-25 are currently under examination.

The requirement is still deemed proper and is therefore made FINAL.

Priority

1. This application 10/591,248 field 11/27/2006, the filed Oath and Declaration filed on 11/27/2006 claims benefit of foreign priority of JAPAN 2004-061291 filed on 03/04/2004 and JAPAN 2004-062812 filed on 03/05/2004. The Examiner acknowledges that Applicant has submitted on 08/31/2006 a certified copy of JAPAN 2004-061291 filed on 03/04/2004 and JAPAN 2004-062812 filed on 03/05/2004 under requirement of 35 U.S.C. 119 (a-d) conditions. However, it is noted that, the certified copy of JAPAN 2004-061291 filed on 03/04/2004 and JAPAN 2004-062812 filed on 03/05/2004 are in Japanese. Therefore, without a certified translation of JAPAN 2004-061291 filed on 03/04/2004 and JAPAN 2004-062812 filed on

03/05/2004, the effective filing date for the instant claims is determined to be 03/03/2005, the filing date of PCT/JP2005/003589. Applicant cannot rely upon the foreign priority papers to overcome the rejection under 35 USC 102 (e) or 102 (a), when applicable, because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claim Objection

2. Claim 20 is objected to for being drawn to a non-elected invention. Specifically, Applicants have elected "Group X, claims 20-25, drawn a yeast transformant which is introduced with a polyhydroxyalkanoic acid synthase gene and an acetoacetyl CoA reductase gene, and both of these genes being introduced in 2 or more copies" as elected invention recited in claim 20 and as such, claim 20 and dependent claims 21-25 are examined only to the extent that they read on yeast transformant with both a polyhydroxyalkanoic acid synthase gene and an acetoacetyl CoA reductase gene. Applicants are required to delete the non-elected subject matter (i.e. yeast transformant with either a polyhydroxyalkanoic acid synthase gene or an acetoacetyl CoA reductase gene being introduced in 2 or more copies) from the instant claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 20 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by **Breuer et al.** (Breuer et al., Yeasts as Producers of Polyhydroxyalkanoates: Genetic Engineering of *Saccharomyces cerevisiae, Macromolecular Bioscience, Germany* 2(8): 380-386, 2002; this reference is cited in the IDS filed by Applicant on 10/15/2007).

Claim 20 is directed to a yeast transformant which is introduced with a polyhydroxyalkanoic acid synthase gene and an acetoacetyl CoA reductase gene, and both of these genes being introduced in 2 or more copies.

Breuer et al. teaches using *Saccharomyces cerevisiae* (baker's yeast) as a bioreactor for production of polyhydroxyalkanoates (PHAs). Breuer et al. teaches that *phaC* gene encodes polyhydroxyalkanoic acid (PHA) synthase, and *phbB* gene encodes acetyl-CoA reductase.

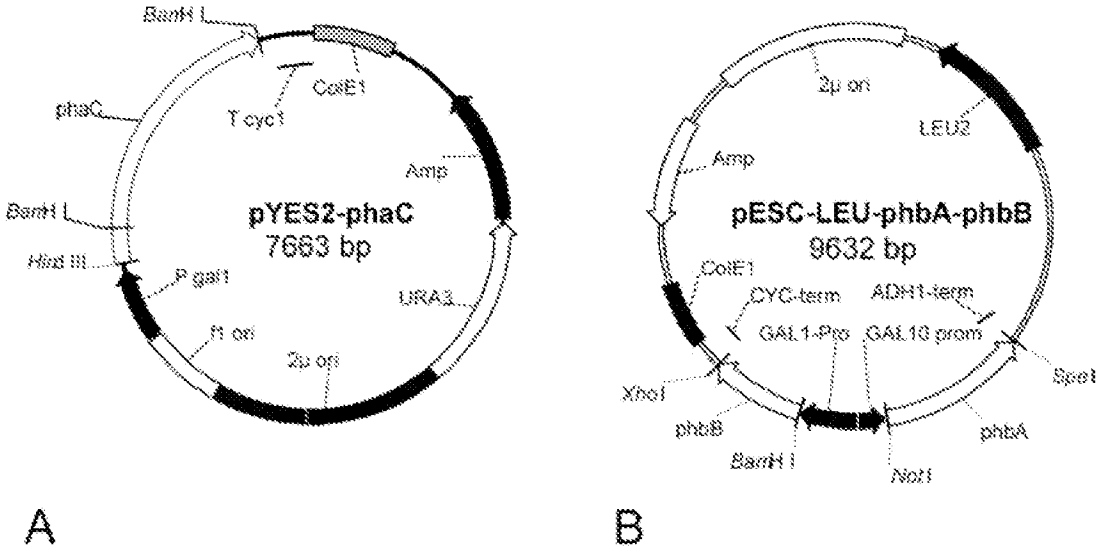

Figure 1. Physical maps of the expression vectors used in this study: (A) pYES2–phaC; (B) pESC–LEU–phbA–phbB.

Breuer et al. the cloning of *phaC* gene by inserting the gene between the *S. cerevisiae* promoter and terminator sequences and expresses the gene in a high copy plasmid with 2μ replication origin (YES2-phaC), and by the same procedure *phbB* gene is cloned and expressed

from a high copy plasmid with 2μ replication origin (pESC-LEU-phbA-phbB), and (See Plasmid constructs and transformation procedure, pages 381-382, and Figure 1, shown above, Breuer et al., 2002).

Thus, Breuer et al. clearly anticipates claims 20 and 22 of instant application.

Claim Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Breuer et al.** (Breuer et al., Yeasts as Producers of Polyhydroxyalkanoates: Genetic Engineering of *Saccharomyces cerevisiae, Macromolecular Bioscience, Germany* 2(8): 380-386, 2002; This reference is cited in the IDS filed by Applicant on 10/15/2007) in view of **Marchesini et al.** (Marchesini et al., Modification of the monomer composition of polyhydroxyalkanoate synthesized in *Saccharomyces cerevisiae* expressing variants of the beta-oxidation-associated multifunctional enzyme, *Appl Environ Microbiol.* 69(11):6495-9, 2003).

Claim 20 is directed to a yeast transformant which is introduced with a poly-hydroxy-alkanoic acid synthase gene and an acetoacetyl CoA reductase gene, and both of these genes being introduced in 2 or more copies. Claim 21 is directed to the yeast transformant according to claim 20, wherein a peroxisome-targeting signal is added to a polyhydroxyalkanoic acid synthase

gene and an acetoacetyl CoA reductase gene.

Breuer et al. teaches using *Saccharomyces cerevisiae* (baker's yeast) as a bioreactor for production of polyhydroxyalkanoates (PHAs). Breuer et al. teaches that *phaC* gene encodes polyhydroxyalkanoic acid (PHA) synthase, and *phbB* gene encodes acetyl-CoA reductase. Breuer et al. the cloning of *phaC* gene by inserting the gene between the *S. cerevisiae* promoter and terminator sequences and expresses the gene in a high copy plasmid with 2μ replication origin (YES2-phaC), and by the same procedure *phbB* gene is cloned and expressed from a high copy plasmid with 2μ replication origin (pESC-LEU-phbA-phbB), and (See Plasmid constructs and transformation procedure, pages 381-382, and Figure 1, shown below, Breuer et al., 2002).

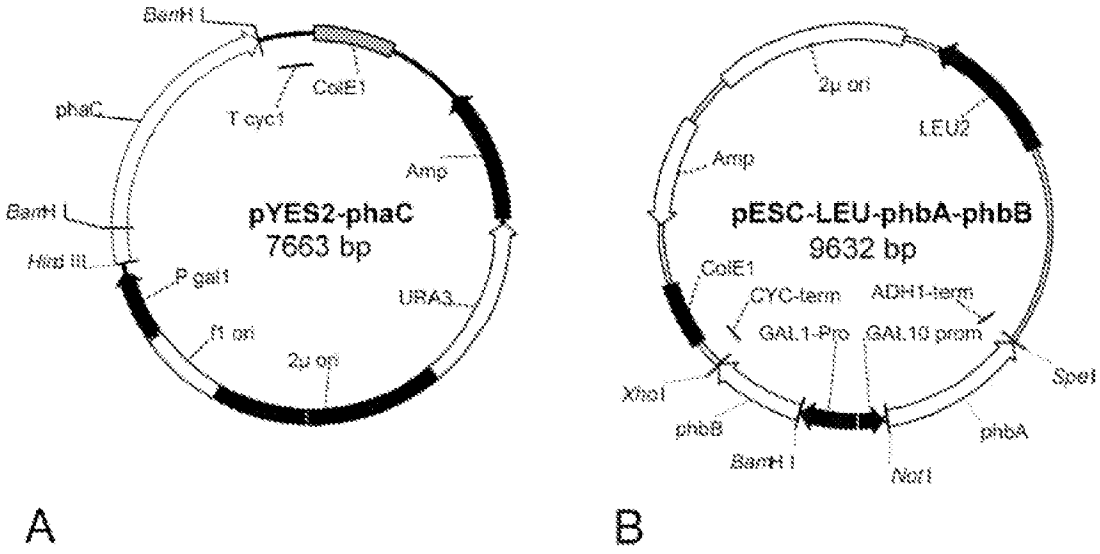

Figure 1. Physical maps of the expression vectors used in this study: (A) pYES2–phaC; (B) pESC–LEU–phbA–phbB.

Breuer et al. does not teach a peroxisome-targeting signal is added to a poly-hydroxy-alkanoic acid synthase gene and an acetoacetyl CoA reductase gene, as recited in claim 21 of instant application.

Marchesini et al. teaches polyhydroxyalkanoates (PHAs) represent a family of polyesters having thermoplastic and elastomeric properties that are naturally synthesized as intracellular inclusions by a wide variety of bacteria, and PHAs can be defined into two main classes based on their monomer compositions. Short-chain-length PHAs are composed mainly of hydroxy acids ranging from 3 to 5 carbons and have properties of plastics, while medium-chain-length PHAs (MCL-PHAs) contain hydroxy acid monomers ranging from 6 to 16 carbons and have properties of elastomers. Marchesini et al. teaches the ability of the terminal peptide Ser-Arg-Met and of the 34-amino-acid peptide from the *B. napus* ICL (isocitrate lyase) as peroxisome targeting signal (PTS), which can target heterologous proteins to the peroxisome of *S. cerevisiae* and genetic modifications of gene involving in regulation of β-oxidation cycle in peroxisome, which can in turn affect the relative production of PTS-modified medium-chain-length PHAs (MCL-PHAs) and Short-chain-length PHAs.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time of the invention to combine the teachings of Breuer et al. regarding a yeast transformant as a bioreactor, which harbors a polyhydroxyalkanoic acid synthase gene and an acetoacetyl CoA reductase gene, and both of these genes being introduced in 2 or more copies, for production of polyhydroxyalkanoates (PHAs), with the teachings of Marchesini et al. regarding modulation of relative production of medium-chain-length PHAs (MCL-PHAs) and short-chain-length PHAs by adding peroxisome targeting signal (PTS) to a polyhydroxyalkanoic acid synthase and an acetoacetyl CoA reductase, to arrive at the claimed yeast transformant recited in claim 21 of instant application.

One having ordinary skill in the art would have been motivated to combine the teachings of Breuer et al. with the teachings of Marchesini et al. because Marchesini et al. teaches that addition of peroxisome targeting signal (PTS) to a polyhydroxyalkanoic acid synthase and an acetoacetyl CoA reductase can modulate relative production between medium-chain-length PHAs (MCL-PHAs) and short-chain-length PHAs. Marchesini et al. further teaches different properties and uses of short-chain-length PHAs (having properties of plastics), while medium-chain-length PHAs (having properties of elastomers).

There would have been a reasonable expectation of success given (i) successful demonstration of using yeast *S. cerevisiae* as a bioreactor for production PHAs by expression of a polyhydroxyalkanoic acid synthase gene and an acetoacetyl CoA reductase gene, by the teachings of Breuer et al., and (ii) the demonstration of the effect of addition of peroxisome targeting signal (PTS) in regulation of relative production of short-chain-length PHAs (having properties of plastics), while medium-chain-length PHAs (having properties of elastomers), by the teachings of Marchesini et al.

Thus, the claimed invention as a whole was clearly *prima facie* obvious

5. Claims 20 and 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Breuer et al.** (Breuer et al., Yeasts as Producers of Polyhydroxyalkanoates: Genetic Engineering of *Saccharomyces cerevisiae, Macromolecular Bioscience, Germany* 2(8): 380-386, 2002; This reference is cited in the IDS filed by Applicant on 10/15/2007) in view of **Fallon et al.** (WO 99/04014, publication date, 01/28/1999; This reference is cited in the IDS filed by Applicant on 11/27/2006).

Claim 20 is directed to a yeast transformant which is introduced with a polyhydroxyalkanoic acid synthase gene and an acetoacetyl CoA reductase gene, and both of these genes being introduced in 2 or more copies. Claim 23 is directed to the yeast transformant according to claim 20, wherein the yeast belongs to the genus *Candida*. Claim 24 is directed to the yeast transformant according to claim 20, wherein the yeast is the *maltosa* species. Claim 25 is directed to the yeast transformant according to claim 20, wherein the yeast is *Candida maltosa.*

Breuer et al. teaches using *Saccharomyces cerevisiae* (baker's yeast) as a bioreactor for production of polyhydroxyalkanoates (PHAs). Breuer et al. teaches that phaC gene encodes polyhydroxyalkanoic acid (PHA) synthase, and *phbB* gene encodes acetyl-CoA reductase. Breuer et al. the cloning of *phaC* gene by inserting the gene between the *S. cerevisiae* promoter and terminator sequences and expresses the gene in a high copy plasmid with 2μ replication origin (YES2-phaC), and by the same procedure *phbB* gene is cloned and expressed from a high copy plasmid with 2μ replication origin (pESC-LEU-phbA-phbB), and (See Plasmid constructs and transformation procedure, pages 381-382, and Figure 1, Breuer et al., 2002).

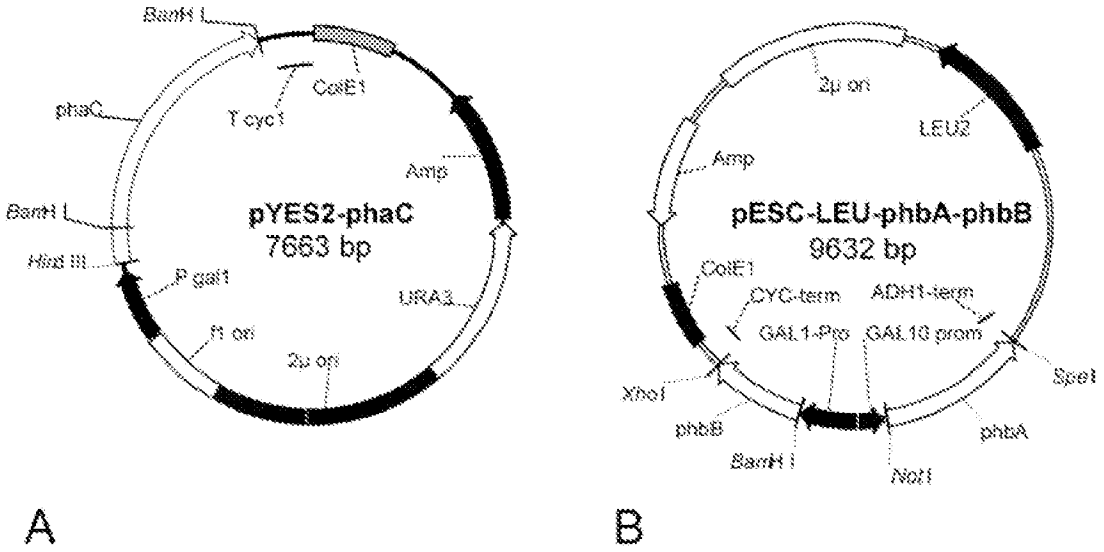

Figure 1. Physical maps of the expression vectors used in this study: (A) pYES2–phaC; (B) pESC–LEU–phbA–phbB.

Breuer et al. does not teach wherein the yeast belongs to the genus of *Candida* as recited in claim 23, wherein the yeast is the *maltosa* species as recited in claim 24, and wherein the yeast is *Candida maltosa* as recited in claim 25 of instant application.

Fallon et al. teaches transformed yeast strains and their use for the production of mono-terminal and di-terminal carboxylates, and a bioprocess for converting aliphatic compounds, of the form CH3(CH2)nCH3 where n = 4 to 20, to monoterminal and diterminal carboxylates, which include polyhydroxyalkanoates (PHAs), using genetically-engineered organisms. Specifically, Fallon et al. teaches a process for expressing alkane hydroxylating activity in genetically-engineered yeast *Candida maltosa*, a process to produce genetically transformed *Candida maltosa* strains that have enhanced cytochrome P450 activity and/or gene disruptions in the beta-oxidation pathway, which in turn increases the yield and selectivity of a bioprocess for conversion of alkanes to momo- and diterminal carboxylates (See title, abstract, and lines 32-35, page 11, claims 16-18, Fallon et al., 1999).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time of the invention to combine the teachings of Breuer et al. regarding a yeast transformant as a bioreactor, which harbors a polyhydroxyalkanoic acid synthase gene and an acetoacetyl CoA reductase gene, and both of these genes being introduced in 2 or more copies, for production of polyhydroxyalkanoates (PHAs), with the teachings of Fallon et al. regarding generation of genetically-engineered yeast *Candida maltosa* with gene disruptions in the beta-oxidation pathway, and the use of these *Candida maltosa* strains for enhanced production of momo- and diterminal carboxylates, which include polyhydroxyalkanoates (PHAs).

One having ordinary skill in the art would have been motivated to combine the teachings of Breuer et al. with the teachings of Fallon et al. because (i) Breuer et al. teaches that the yield for production of polyhydroxyalkanoates (PHAs) using *S. cerevisiae* as a bioreactor is less than ideal for overproduction of PHAs (See Discussion son pages 384-385, Breuer et al., 2002), and (ii) Fallon et al. teaches that genetically-engineered yeast *Candida maltosa* with gene disruptions in the beta-oxidation pathway can enhance production of momo- and diterminal carboxylates, which include polyhydroxyalkanoates (PHAs).

There would have been a reasonable expectation of success given (i) successful demonstration of using yeast *S. cerevisiae* as a bioreactor for production PHAs by expression of a polyhydroxyalkanoic acid synthase gene and an acetoacetyl CoA reductase gene, by the teachings of Breuer et al., and (ii) the demonstration of yeast *Candida maltosa* with gene disruptions in the beta-oxidation pathway enhances production of momo- and diterminal carboxylates, by the teachings of Fallon et al.

Thus, the claimed invention as a whole was clearly *prima facie* obvious

Conclusion

6. No claim is allowed.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent examiner, Peter Paras, Jr. can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private

PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Wu-Cheng Winston Shen/
Patent Examiner
Art Unit 1632